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L8	l7 and link$	15	L8
L7	L6 and electrophore$3	15	L7
L6	L5 and kit$1	16	L6
L5	L4 and capture$1	16	L5
L4	L3 and cleav$	27	L4
L3	L1 and (tag$ or label$ or reportor$1)	34	L3
L2	L1 and kit	30	L2
L1	antibody binding compound$1	35	L1

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☐ 1. 6395889 . 09 Sep 99; 28 May 02. Nucleic acid molecules encoding human protease homologs. Robison; Keith E.. 536/23.2; 435/252.3 435/320.1 435/69.1 536/23.5. C12N015/57 C12N015/12 C12N009/64 C12N015/79.

☑ 2. 6391569 . 18 Sep 96; 21 May 02. Method to detect Dirofilaria immitis infection. Grieve; Robert B., et al. 435/7.22; 424/151.1 424/191.1 424/192.1 424/269.1 435/342 435/69.1 435/7.1 435/7.92 435/7.93 435/7.94 435/7.95 436/501 436/518 436/528 530/350 530/387.1 530/388.6 530/403. G01N033/53 G01N033/569 G01N033/544 G01N033/543.

☐ 3. 6331427 . 26 Mar 99; 18 Dec 01. Protease homologs. Robison; Keith E.. 435/226; 435/23 435/252.3 435/6 435/69.1 435/7.1 536/23.2. C12N009/64 C12N015/57 C12N015/79 C12Q001/37 C12Q001/38.

☐ 4. 6271014 . 14 Dec 98; 07 Aug 01. Mammalian proteinases; related reagents and methods. de Saint-Vis; Blandine Marie, et al. 435/226; 435/189 435/219 530/350 536/23.2. C12N009/50 C12N009/04.

☑ 5. 6242586 . 12 Dec 97; 05 Jun 01. Mammalian cell surface antigens: related reagents. Gorman; Daniel M., et al. 536/23.4; 424/185.1 435/252.1 435/320.1 435/325 435/348 435/352 435/354 435/363 435/366 435/6 435/69.3 435/91.1 530/350 530/395 530/402 536/23.5 536/24.3 536/24.33. A61K038/17 C07H021/04 C12N005/10 C12P019/34.

☐ 6. 6193963 . 21 Aug 97; 27 Feb 01. Method of treating tumor-bearing patients with human plasma hyaluronidase. Stern; Robert, et al. 424/94.6; 424/94.61 424/94.62 514/12 514/2. A61K038/00 A61K038/46 A61K038/47 A01N037/18.

☐ 7. 6140076 . 05 Dec 97; 31 Oct 00. Ig superfamily `dlair` receptors expressed in monocytes. Adema; Gosse Jan, et al. 435/69.1; 435/252.3 435/254.11 435/320.1 435/325 435/348 435/352 435/366 435/6 435/69.7 435/91.1 435/91.2 514/2 530/350 536/23.5 536/24.31. C12N015/12 C07N014/705 A61K038/17.

☑ 8. 6124436 . 13 Feb 96; 26 Sep 00. Purified mammalian monocyte antigens and related reagents. McClanahan; Terrill K., et al. 530/387.1; 435/326 435/331 435/343 436/512 530/387.9 530/391.1 530/391.3 530/391.7. C07K016/00 C12N005/00 G01N033/563.

☐ 9. 6103525 . 17 Oct 96; 15 Aug 00. Hybridoma cell lines producing monoclonal antibodies that bind to human plasma hyaluronidase. Stern; Robert, et al. 435/326; 435/338 530/388.1. C12N005/12 C07K016/00.

☐ 10. 6069229 . 07 Mar 97; 30 May 00. Mammalian proteinases; oxidoreductases; related reagents. Dowling; Lynette M., et al. 530/300; 435/252.3 435/320.1 435/69.1 435/89. A61K038/00 C12N015/00 C12P021/06 C12P019/30.

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Term	Documents
LINK$	0
LINK.DWPI,EPAB,JPAB,USPT.	453922
LINKA.DWPI,EPAB,JPAB,USPT.	96
LINKAAGE.DWPI,EPAB,JPAB,USPT.	2
LINKAAGES.DWPI,EPAB,JPAB,USPT.	2
LINKAB.DWPI,EPAB,JPAB,USPT.	16
LINKABALE.DWPI,EPAB,JPAB,USPT.	1
LINKABARS.DWPI,EPAB,JPAB,USPT.	1
LINKABE.DWPI,EPAB,JPAB,USPT.	22
LINKABEL.DWPI,EPAB,JPAB,USPT.	1
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Term: L4 and kit

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L5	L4 and kit	1	L5
L4	L3 and link$	1	L4
L3	L2 and cleav$	1	L3
L2	antibody binding near5 compound$1 near5 (tag$1 or label$1 or reporter$1)	2	L2
L1	antibody binding near5 compound$1 near5 (tag$1 or label$1 or reporter$1) near5 cleav$	0	L1

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☑ 1. 5688657. 12 Sep 94; 18 Nov 97. Monoclonal antibodies against human colon carcinoma-associated antigens and uses therefor. Tsang; Kwong Y., et al. 435/7.23; 435/325 435/328 435/329 435/330 435/332 435/344 435/40.51 435/40.52 435/7.1 435/7.2 530/387.1 530/387.3 530/387.5 530/387.7 530/388.1 530/388.8 530/391.1 530/391.3 530/391.7. G01N033/574 G01N033/53 C07K016/30 C07K016/18.

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Term	Documents
KIT.DWPI,EPAB,JPAB,USPT.	82032
KITS.DWPI,EPAB,JPAB,USPT.	24597
(4 AND KIT).USPT,JPAB,EPAB,DWPI.	1
(L4 AND KIT).USPT,JPAB,EPAB,DWPI.	1

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L5: Entry 1 of 1 File: USPT Nov 18, 1997

DOCUMENT-IDENTIFIER: US 5688657 A
TITLE: Monoclonal antibodies against human colon carcinoma-associated antigens and uses therefor

Brief Summary Text (53):
In another embodiment, the present invention includes a kit for selectively characterizing colon, breast, and ovarian carcinomas.

Detailed Description Text (6):
The term "antibody" is meant to include both intact immunoglobulin molecules as well as fragments and derivatives thereof, such as, for example, Fab, Fab', F(ab').sub.2 and Fv, which are capable of binding antigen. These fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody (Wahl et al., J. Nucl. Med. 24:316-325 (1983)). These fragments are produced from intact antibodies using methods well known in the art, for example by proteolytic cleavage with enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab').sub.2 fragments).

Detailed Description Text (7):
A "derivative" of an antibody contains additional chemical moieties not normally a part of the protein. Covalent modifications of the protein are included within the scope of this invention. Such modifications may be introduced into the molecule by reacting targeted amino acid residues of the antibody with an organic derivatizing agent that is capable of reacting with selected side chains or terminal residues. For example, derivatization with bifunctional agents, well-known in the art, is useful for cross-linking the antibody or fragment to a water-insoluble support matrix or to other macromolecular carriers.

Detailed Description Text (11):
The chimeric antibodies of the invention comprise individual chimeric heavy (H) and light (L) immunoglobulin chains. The chimeric H chain comprises an antigen-binding region derived from the H chain of a non-human antibody specific for the epitope recognized by 33.28 or 31.1, which is linked to at least a portion of a human H chain C region (C.sub.H).

Detailed Description Text (12):
A preferred chimeric L chain comprises an antigen-binding region derived from the L chain of either the 33.28 or 31.1 mAb, linked to at least a portion of a human L chain C region (C.sub.L).

Detailed Description Text (13):
Alternatively, a preferred chimeric H chain comprises an antigen-binding region derived from the L chain of either the 33.28 or 31.1 mAb, linked to at least a portion of a human L chain C region (C.sub.H).

Detailed Description Text (16):
The invention also provides for "derivatives" of the monoclonal or chimeric antibodies, which term includes those proteins encoded by truncated or modified genes to yield molecular species functionally resembling the immunoglobulin fragments. The modifications include, but are not limited to, addition of genetic sequences coding for cytotoxic proteins such as plant and bacterial toxins. The fragments and derivatives can be produced from prokaryotlc or eukaryotic hosts, as described herein by recombinant means. Alternatively, the fragments and derivatives may be produced by chemical means, such as proteolytic cleavage of intact immunoglobulin molecules, or

other chemical modifications or derivatizations known in the art. Such derivatized moieties may improve the solubility, absorption, biological half-life, and the like. The moieties may alternatively eliminate or attenuate any undesirable side effect of the antibody protein. Moieties capable of mediating such effects are disclosed, for example, in Remington's Pharmaceutical Sciences, 16th ed., Hack Publishing Co., Easton, Pa. (1980).

Detailed Description Text (27):
Thus, in a preferred embodiment, a fused gene is created which comprises a first DNA segment that encodes at least the antigen-binding region of non-human origin, such as a functionally rearranged V region with joining (J) segment, linked to a second DNA segment encoding at least a part of a human C region. This fusion can be accomplished by the polymerase chain reaction, as reported by Fernando et al., Miami Symp. Short Reports 3: 88, 1993.

Detailed Description Text (33):
4. Construction of complete H or L chain coding sequences by linkage of the cloned specific V region gene segments to cloned human C region gene, as described above;

Detailed Description Text (37):
One common feature of all immunoglobulin H and L chain genes and their encoded mRNAs is the J region. H and L chain J regions have different sequences, but a high degree of sequence homology exists (greater than 80%) among each group, especially near the C region. This homology is exploited in this method and consensus sequences of H and L chain J regions may be used to design oligonucleotides for use as primers for introducing useful restriction sites into the J region for subsequent linkage of V region segments to human C region segments.

Detailed Description Text (38):
C region cDNA vectors prepared from human cells can be modified by site-directed mutagenesis to place a restriction site at the analogous position in the human sequence. For example, one can clone the complete human kappa chain C (C.sub.k) region and the complete human gamma-1 C region (C.sub.gamma-1). In this case, the alternative method based upon genomic C region clones as the source for C region vectors would not allow these genes to be expressed in bacterial systems where enzymes needed to remove intervening sequences are absent. Cloned V region segments are excised and ligated to L or H chain C region vectors. Alternatively, the human C.sub.gamma-1 region can be modified by introducing a termination codon thereby generating a gene sequence which encodes the H chain portion of an Fab molecule. The coding sequences with linked V and C regions are then transferred into appropriate expression vehicles for expression in appropriate hosts, prokaryotic or eukaryotic.

Detailed Description Text (39):
Two coding DNA sequences are said to be "operably linked" if the linkage results in a continuously translatable sequence without alteration or interruption of the triplet reading frame. A DNA coding sequence is operably linked to a gene expression element if the linkage results in the proper function of that gene expression element to result in expression of the coding sequence.

Detailed Description Text (59):
Many vector systems are available for the expression of cloned H and L chain genes in mammalian cells (see Glover, D. M., ed., DNA Cloning, Vol. II, pp. 143-238, IRL Press, 1985). Different approaches can be followed to obtain complete H.sub.2 L.sub.2 antibodies. As discussed above, it is possible to co-express H and L chains in the same cells to achieve intracellular association and linkage of H and L chains into complete tetrameric H.sub.2 L.sub.2 antibodies. The co-expression can occur by using either the same or different plasmids in the same host. Genes for both H and L chains can be placed into the same plasmid, which is then transfected into cells, thereby selecting directly for cells that express both chains. Alternatively, cells may be transfected first with a plasmid encoding one chain, for example the L chain, followed by transfection of the resulting cell line with an H chain plasmid containing a second selectable marker. Cell lines producing H.sub.2 L.sub.2 molecules via either route could be transfected with plasmids encoding additional copies of H, L, or H plus L chains in conjunction with additional selectable markers to generate cell lines with enhanced properties, such as higher production of assembled H.sub.2 L.sub.2 antibody

molecules or enhanced stability of the transfected cell lines.

Detailed Description Text (88):
One of the ways in which the antibody of the present invention can be detectably labelled is by linking the same to an enzyme and use in an enzyme immunoassay (EIA) or enzyme-linked immunosorbent assay (ELISA). This enzyme, when subsequently exposed to its substrate, will react with the substrate generating a chemical moiety which can be detected, for example, by spectrophotometric, fluorometric or by visual means. In an alternate embodiment, the enzyme is used to label a binding partner for the antibody of the invention. Such a binding partner may be an antibody against the constant or variable region of the antibody of the invention, such as a heterologous anti-mouse immunoglobulin antibody. Alternatively, the binding partner may be a non-antibody protein capable of binding to the antibody of the present invention, such as staphylococcal protein A, or streptococcal protein G.

Detailed Description Text (91):
It is also possible to label the antibodies or binding partners with a fluorescent compound. When the fluorescently labelled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labelling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and flourescamine.

Detailed Description Text (96):
In situ detection may be accomplished by removing a histological specimen from a patient, and providing the labelled antibody, or the unlabelled antibody plus a labelled binding partner to such a specimen. Through the use of such a procedure, it is possible to determine not only the presence of the antigen but also its distribution in the examined tissue. Using the present invention, those of ordinary skill will readily perceive that any of a wide variety of histological methods (such as staining procedures) can be modified in order to achieve such in situ detection. Such methods include, for example, immunohistochemical staining procedures. In a preferred embodiment, an avidin-biotin immunoperoxidase staining system can be used, and a kit utilizing this system is also contemplated.

Detailed Description Text (97):
The kit employing mAbs or chimeric antibodies of the present invention can be used for immunohistochemical evaluation of colon, breast, and ovarian carcinoma. Indications for tissue study are to evaluate subpopulations of tumor cells that express the antigens defined by mAbs 31.1 and 33.28.

Detailed Description Text (98):
The colon kit is comprised of the reagents necessary for immunohistochemical analysis as follows:

Detailed Description Text (103):
Similar kits can be employed for the immunohistochemical analysis of breast and ovarian carcinoma.

Detailed Description Text (105):
The kit contemplated herein can be used to study fully developed colon, carcinoma, polyps in transformation to define the extent of malignant transformation, benign polyps to see if a site of transformation has been missed and inflammatory bowel disease to evaluate any sites of undetected transformation. Similar kits can be employed to study breast and ovarian carcinomas.

Detailed Description Text (106):
Another kit similar to the above kit is also contemplated which uses all five mAbs to colon carcinoma in order to evaluate all subpopulations of tumors and as such has the capability to type and cross-match the lesions.

Detailed Description Text (130):
An enzyme-linked immunosorbent assay (ELISA), described by Tsang et al., JNCI 77:1175 (1986), was used for the detection of hybridoma clones producing antibodies specific for the CCAA. CCAA (100 n/well) was immobilized on polystyrene microplates. Antibodies

present in the test supernatants were allowed to bind to the immobilized antigens. The presence of the bound murine mAbs was detected with peroxidase-conjugated second antibodies, specific for mouse immunoglobulins, followed by the chromogenic substrate for peroxidase, O-phenyldiamine. Wells showing color reactions yielding Absorbances .gtoreq.0.500 units were scored as positive. Negative controls gave values of 0.01 to 0.09 units.

CLAIMS:

28. A kit for the immunohistochemical detection of colon carcinoma comprising:

(a) mouse monoclonal antibody 31.1 (ATCC HB-12314);

(b) reagents for immunoperoxidase and secondary antibody;

(c) immunoperoxidase; and

(d) colorizing reagents.

29. A kit for the immunohistochemical detection of colon carcinoma comprising:

(a) mouse monoclonal antibody 33.28 (ATCC HB-12315);

(b) reagents for immunoperoxidase and secondary antibody;

(c) immunoperoxidase; and

(d) colorizing reagents.

30. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain an antibody to said antigen or an active component thereof, and a second container adapted to contain a second antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

31. A kit according to claim 30 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

32. A kit according to claim 30 wherein the reporter molecule is an enzyme.

33. A kit according to claim 30 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

34. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain monoclonal antibody 31.1 (ATCC HB-12314) to said antigen and a second container adapted to contain a second antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

35. A kit according to claim 34 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

36. A kit according to claim 32 wherein the reporter molecule is an enzyme.

37. A kit according to claim 33 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

38. A compartmentalized kit for the detection of a human colon carcinoma-associated antigen, wherein the antigen has the following characteristics:

(a) said antigen is purified to the extent that the membrane fractions are free of HL-A antigen and are substantially free from non-immunogenic glycoprotein fractions;

(b) said antigen is not detectable on normal colon cancer free human tissues;

(c) said antigen is not detectable on human carcinoma cells other than colon carcinoma cells;

(d) said antigen is specifically immunogenic in humans; and

(e) said antigen induces an immune response in humans having colon carcinoma which is expressed as cell mediated immunity,

said kit comprising a first container adapted to contain monoclonal antibody 33.28 (ATCC HB-12315) to said antigen and a second container adapted to contain a second antibody to said antigen or an active component thereof, said second antibody being labeled with a reporter molecule capable of giving a detectable signal.

39. A kit according to claim 38 wherein the reporter molecule is a radioisotope, an enzyme, a fluorescent molecule, a chemiluminescent molecule or a bioluminescent molecule.

40. A kit according to claim 38 wherein the reporter molecule is an enzyme.

41. A kit according to claim 38 wherein the kit further comprises a third container adapted to contain a substrate for the enzyme.

50. A kit for the immunohistochemical detection of colon carcinoma comprising:

(a) mouse/human chimeric antibody Chi #1 (ATCC CRL-12316);

(b) reagents for immunoperoxidase and secondary antibody;

immunoperoxidase; and

(d) colorizing reagents.